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Research paper

Enhancement of griseofulvin release from liquisolid compacts

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ABSTRACT

The potential of hydrophilic aerogel formulations and liquisolid systems to improve the release of poorly soluble drugs was investigated using griseofulvin as model drug. The in vitro release rates of this drug formulated as directly compressed tablets containing crystalline griseofulvin were compared to aerogel tablets with the drug adsorbed onto hydrophilic silica aerogel and to liquisolid compacts containing the drug dissolved or suspended in PEG 300. Furthermore, the commonly used carrier and coating materials in liquisolid systems Avicel® and Aerosil® were replaced by Neusilin®, an amorphous magnesium aluminometasilicate with an extremely high specific surface area of 339 m^2/g to improve the liquisolid approach.

Both the liquisolid compacts containing the drug dissolved in PEG 300 and the aerogel tablets showed a considerably faster drug release than the directly compressed tablets. With liquisolid compacts containing the drug suspended in PEG 300, the release rate increased with rising fraction of dissolved drug in the liquid portion. It could be shown that Neusilin® with its sevenfold higher liquid adsorption capacity than the commonly used Avicel® and Aerosil® allows the production of liquisolid formulations with lower tablet weights.

1. Introduction

Since the implementation of combinatorial chemistry and high throughput screening for the investigation of new chemical entities, the molecular weight and lipophilicity of drugs increase and this in turn decreases water solubility [1]. Especially poorly soluble, highly permeable active pharmaceutical ingredients (BCS Class II drugs) represent a technological challenge, as their poor bioavailability is solely caused by poor water solubility resulting in low drug absorption [2]. Therefore, new technologies increasing the solubility and thus drug release are looked for. Release enhancement of poorly soluble drugs may be achieved by an increase in the drug solubility, the drug surface area, or by formulating the drug in its dissolved state: Several methodologies such as micronization [3], co-grinding [4,5], formulation of inclusion complexes [6], solid dispersions [7,8], and lipid based formulations [9] such as self-emulsifying drug delivery systems (SEDDS) have been introduced with different success.

Adsorption of drugs to hydrophilic silica aerogels has been shown to be a promising technique for drug release enhancement [10–12]. This methodology also allows a long-time stabilization of amorphous drugs. Upon contact with fluids, the structure of hydrophilic aerogels collapses and a fast release of the loaded drug takes place.

One of the most promising approaches for release enhancement is the liquisolid technique [13–19]. Liquisolid systems as described by Spireas [13,14] are composed of a non-volatile, water miscible liquid vehicle, solid drug particles, and selected excipients, namely the carrier and coating materials. The liquid portion, which can be a liquid drug, a drug suspension, or a drug solution in suitable non-volatile liquid vehicles, is incorporated into the porous carrier material. Once the carrier is saturated with liquid, a liquid layer is formed on the particle surface, which is instantly adsorbed by the fine coating particles. Thus, an apparently dry, free flowing, and compressible powder is obtained. Liquisolid compacts of poorly soluble drugs containing the drug dissolved or suspended in a solubilizing liquid vehicle provide enhanced drug release due to an increased drug solubility, a high surface area of the drug, and an improved wettability of the drug particles [20,21]. Accordingly, this optimized drug release allows an improved drug absorption in the gastrointestinal tract and thus a higher oral bioavailability [22,23].

Stability studies with liquisolid systems containing various drugs [18,24–26] showed that storage at different conditions neither had an effect on the hardness nor on the release profiles of liquisolid compacts. This indicates that the technology is a

Abbreviations: BCS, biopharmaceutics classification system; SEDDS, self-emulsifying drug delivery system; PEG, polyethylene glycol; RH, relative humidity; LS, liquisolid; RESS, rapid expansion from supercritical solutions.

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promising technique for release enhancement, which is not associated with any physical stability issues.

Besides drug release enhancement, the liquisolid approach is a promising technique because of the simple manufacturing process, low production costs, and the possibility of industrial manufacture due to the good flow and compaction properties of the liquisolid formulations.

To calculate the required amount of powder excipients (carrier and coating materials), a mathematical approach for the formulation of liquisolid systems has been developed by Spireas [27].

Depending on the excipient ratio R of the powder substrate, an acceptably flowing and compressible liquisolid system can be obtained only if a maximum liquid load, named "liquid load factor" (L_f), is not exceeded.

The terms "acceptable flow" and "acceptable compressibility" imply the desired and thus preselected flow and compaction properties, which must be met by the final liquisolid formulation.

R represents the ratio between the mass of the carrier (Q) and the coating (q) materials present in the formulation:

$$R = Q/q \quad (1)$$

L_f represents the ratio between the mass of the liquid portion W and the carrier materials Q:

$$L_f = W/Q \quad (2)$$

With the desired amount of liquid, the amount of carrier and coating material can be calculated if the liquid load factor L_f is known.

The aim of the present study was to compare drug release from several tablet formulations using griseofulvin as model drug. The poorly soluble antifungal drug was formulated as conventional tablets containing crystalline griseofulvin, as aerogel tablets containing the drug adsorbed to hydrophilic silica aerogel, and as liquisolid compacts containing the drug dissolved in PEG 300. Liquisolid compacts containing the drug suspended in PEG 300 were investigated with regard to the influence of drug content in the liquid portion on drug release. Furthermore, the commonly used carrier and coating materials in liquisolid systems Avicel® and Aerosil®, respectively, were replaced by Neusilin® to improve the liquisolid approach. Due to its extremely high specific surface area of 339 ± 1 m^2/g as well as its good flow and tableting properties [28], this magnesium aluminometasilicate was assumed to allow a considerably higher liquid load factor, thereby enabling the preparation of liquisolid compacts with lower tablet weights.

2. Materials and methods

2.1. Materials

Griseofulvin, Fagron, Barsbüttel, Germany; Carbon dioxide (purity 99.9%), AGA Gas, Hamburg, Germany; hydrophilic silica aerogel microspheres, mean particle size 300 μm [29]; polyethylene glycol 300 (PEG 300), glycerol, and propylene glycol, Fagron, Barsbüttel, Germany; Avicel® PH200 (microcrystalline cellulose), FMC BioPolymer, Cork, Ireland; Aerosil® 200 (colloidal silica), Evonik, Darmstadt, Germany; Neusilin® US2 (magnesium aluminometasilicate), Fuji Chemical Industry, Toyama, Japan; Kollidon® CL (crospovidone), BASF, Ludwigshafen, Germany. All other reagents used were of analytical grade.

2.2. Determination of the particle size of the drug raw material

The particle size distribution of griseofulvin was determined in triplicate by laser diffraction using a dry dispersing system with a feeding air pressure of 1 bar (HELOS equipped with RODOS, Sympatec, Clausthal-Zellerfeld, Germany).

2.3. Solubility studies

The solubility of griseofulvin in three non-volatile liquid vehicles that are commonly used for the formulation of liquisolid compacts, namely, propylene glycol, polyethylene glycol 300 (PEG 300), and glycerol was determined by preparation of saturated solutions of the drug in these solvents and measuring their drug concentration: Excess griseofulvin was stirred in the above mentioned solvents for 48 h at 21 °C. Accurately weighed quantities of the filtered supernatants were further diluted with methanol and analyzed spectrophotometrically at 291 nm for their drug content. From these results, the solubility of griseofulvin (in percent [w/w]) in the respective liquid vehicle was calculated. Each experiment was carried out in triplicate.

2.4. Loading of silica aerogel microspheres with griseofulvin

Loading of silica aerogel microspheres with griseofulvin was performed by adsorption of the drug from its solution in supercritical carbon dioxide (solubility of griseofulvin in carbon dioxide: 1.6×10^{-3}% [30]).

To deposit the drug onto silica aerogel microspheres, the following procedure was used: A weighed amount of drug and aerogel microspheres, each wrapped in a filter paper, was placed in an autoclave (250 ml, built at the Hamburg University of Technology, Germany). The autoclave was sealed, heated to 40 °C, and carbon dioxide was pumped inside until a pressure of 180 bars was reached [31,32]. Under these conditions, the drug was completely dissolved and thus, adsorption to the aerogel took place. After 48 h, the pressure was released and the drug-loaded aerogel microspheres (300 μm) were removed. In previous studies, it could be shown by visual evaluation as well as electron microscopy that during impregnation of the aerogel with drug no crystallization occurs in the pores of the aerogel [30].

To determine the percentage of drug in the loaded aerogel, a weighed amount of aerogel microspheres was dispersed in methanol. The solution was stirred for at least 20 min to ensure complete dissolution of the drug. The concentration of the drug in methanol was analyzed spectrophotometrically at 291 nm (1 cm quartz cells, 8453, Agilent Technologies, Santa Clara, USA). Based on these data, the percentage of drug in the loaded aerogel was calculated. Each experiment was carried out in triplicate.

2.5. Preparation of directly compressed tablets

A conventional tablet formulation with micronized griseofulvin and an aerogel tablet formulation with griseofulvin adsorbed to hydrophilic silica aerogel were prepared with each tablet containing Kollidon® CL as disintegrant, Avicel® as binder, and 1.5 mg of drug. The percentage of drug of the hydrophilic silica aerogel microspheres was determined to 3.0 ± 0.1% [w/w], and therefore, each tablet contained 50 mg of drug-loaded silica aerogel. To ensure that tablet disintegration is not the rate-limiting step and drug release is not hindered by slow disintegration of the dosage form, 5% [w/w] Kollidon® CL was added to all formulations. All ingredients were mixed for 5 min in a Turbula blender (T2F, Willy A. Bachofen, Muttenz, Switzerland) and compressed into tablets with an instrumented single punch press (EXI, Fette, Schwarzenbek, Germany) equipped with flat faced punches of 10 mm diameter. For each tablet, 300 mg of the powder blends was filled manually into the die and compressed at a compaction speed of 16 strokes/min. The compaction force was adjusted to achieve a minimum tensile strength of 1 MPa [33]. All experiments were performed at 21 °C/45% RH.

2.6. Preparation of liquisolid compacts

Several liquisolid formulations with each sample unit containing 3 mg of griseofulvin (corresponding to 2–5 tablets) were prepared by addition of the liquid portion (0.9–2.3% drug in PEG 300) to the blend of carrier and coating material and mixing in a mortar (Table 1). Finally, Kollidon® CL was added, and the formulations were mixed for 5 min in a Turbula blender. The liquisolid formulations LS-1–LS-10 consisted of Avicel® as carrier and Aerosil® as coating material. Carrier and coating materials were used in a weight ratio of 20:1 (= *R*-value) according to the recommendation of Spireas et al. [34]. A liquid load factor of 0.22 was used in these formulations resulting in acceptable flowability of the blends (maximum angle of slide 33 °C) and sufficient tablet hardness (minimum tensile strength 1 MPa). For the liquisolid formulation LS-N with Neusilin® as carrier as well as coating material, a liquid load factor of 1.58 was used. Despite such a high liquid load factor, the formulation fulfills the required flowability and tablet hardness. The high liquid loading capacity of this magnesium aluminometasilicate may be explained by its extremely high specific surface area of 339 ± 1 m^2/g as well as its good flow and tableting properties [28].

The liquisolid formulations were compacted as described for the directly compressed tablets. However, for the liquisolid compacts, the required amount of powder blend for one tablet was between 300 and 434 mg (Table 1).

Formulations LS-2–LS-10 contained drug suspensions as liquid portion in contrast to LS-1and LS-N which contained a drug solution. For suspensions, the fraction of dissolved drug in the liquid portion is calculated by the ratio of the drug's solubility in the liquid vehicle PEG 300 and the total drug content in the liquid portion present in each formulation (Table 1).

2.7. Disintegration studies

Disintegration time of the investigated tablets was measured with a disintegration tester (ZT 72, Erweka, Heusenstamm, Germany) according to the conditions of the Ph. Eur. for uncoated tablets.

2.8. Drug release studies

Drug release of the tablets was measured according to the Ph. Eur. in phosphate buffer (pH 6.8) using a paddle apparatus (Sotax AT7, Allschwil, Switzerland) at 100 rpm and 37 °C. In each vessel containing 900 ml dissolution medium, one sample unit corresponding to 3 mg of griseofulvin was analyzed. For instance, from formulation LS-1, five tablets were placed in each vessel, whereas for the directly compressed tablets and the LS-N tablets only two tablets were used. Because of the slightly different UV spectrum in phosphate buffer, drug release profiles were recorded spectrophotometrically at 295 nm.

3. Results and discussion

3.1. Particle size of the drug raw material

Poorly soluble, highly permeable active pharmaceutical ingredients such as griseofulvin are classified as BCS Class II drugs. These drugs represent a technological challenge, as their poor bioavailability is solely caused by poor water solubility. BCS Class II drugs are commonly used as micronized materials showing an increased specific surface area and thus a faster drug release. In the present study, micronized griseofulvin with a mean particle size of 9.3 ± 0.1 μm was used as crystalline raw material.

3.2. Solubility of griseofulvin in various non-volatile liquid vehicles

Griseofulvin was found to be poorly soluble in glycerol (0.004 ± 0.000 [% w/w]) and propylene glycol (0.13 ± 0.00 [% w/w]). Its solubility in PEG 300 (0.95 ± 0.00 [% w/w]) was much higher. Thus, to minimize the required amount of liquid, PEG 300 was chosen as liquid vehicle for preparation of griseofulvin liquisolid compacts.

3.3. Dimensions and tensile strength of the investigated tablets

The dimensions and the crushing strength of the liquisolid and the directly compressed tablets are shown in Table 2. Due to

Table 1
Formulation characteristics of the investigated liquisolid compacts with each sample unit containing 3 mg of griseofulvin.

Liquisolid formulation	Total drug content in liquid portion (g/100 g)	Dissolved drug in liquid portion[a] (% w/w)	Amount of liquid portion (mg)	Carrier/coating material (20:1)	Amount of carrier and coating blend (mg)	Disintegrant[b] (mg)	Sample unit weight[c] (mg)
LS-1	0.9	100	333	Avicel®/Aerosil®	1591	102	2026 (5 tablets)
LS-2	1.0	95	300	Avicel®/Aerosil®	1432	91	1823 (5 tablets)
LS-3	1.1	86	273	Avicel®/Aerosil®	1302	82	1657 (4 tablets)
LS-4	1.2	79	250	Avicel®/Aerosil®	1193	76	1519 (4 tablets)
LS-5	1.3	73	231	Avicel®/Aerosil®	1101	70	1402 (4 tablets)
LS-6	1.5	63	200	Avicel®/Aerosil®	955	60	1215 (3 tablets)
LS-7	1.7	56	176	Avicel®/Aerosil®	842	54	1072 (3 tablets)
LS-8	1.9	50	158	Avicel®/Aerosil®	754	47	959 (3 tablets)
LS-9	2.1	45	143	Avicel®/Aerosil®	682	43	868 (2 tablets)
LS-10	2.3	41	130	Avicel®/Aerosil®	623	40	793 (2 tablets)
LS-N	0.9	100	333	Neusilin®/ Neusilin®	222	45	600 (2 tablets)

[a] Solubility of griseofulvin in PEG 300: 0.95 (g/100 g).
[b] 5% (w/w) Kollidon® CL were added to LS-1–LS-10, 7.5% to LS-N.
[c] Each sample unit consisted of several tablets with a weight of 300–434 mg each.

Table 2
Dimensions and tensile strengths of the investigated tablets (means ± SD, $n = 3$).

Formulation	Tablet diameter (mm)	Tablet thickness (mm)	Crushing force (N)	Tensile strength (MPa)
Conventional tablet	10.08 ± 0.02	4.66 ± 0	74 ± 2	1.01 ± 0.02
Aerogel tablet	10.02 ± 0.02	4.52 ± 0.01	74 ± 2	1.04 ± 0.03
LS-1 compact	10.10 ± 0.02	4.32 ± 0.01	68 ± 3	1.00 ± 0.04
LS-2 compact	10.10 ± 0.02	3.95 ± 0.04	62 ± 2	0.99 ± 0.03
LS-3 compact	10.11 ± 0.02	4.44 ± 0.01	71 ± 3	1.01 ± 0.04
LS-4 compact	10.14 ± 0	4.11 ± 0.01	64 ± 3	0.97 ± 0.05
LS-5 compact	10.09 ± 0.02	3.71 ± 0.03	61 ± 3	1.04 ± 0.06
LS-6 compact	10.11 ± 0.02	4.32 ± 0.05	71 ± 5	1.04 ± 0.08
LS-7 compact	10.09 ± 0.01	3.74 ± 0.02	60 ± 3	1.01 ± 0.06
LS-8 compact	10.09 ± 0.01	3.51 ± 0.03	58 ± 3	1.05 ± 0.06
LS-9 compact	10.09 ± 0.01	4.57 ± 0.03	70 ± 5	0.97 ± 0.07
LS-10 compact	10.11 ± 0	4.23 ± 0.03	67 ± 3	0.99 ± 0.05
LS-N compact	10.06 ± 0.01	3.67 ± 0.02	60 ± 1	1.03 ± 0.01

varying tablet weights (see Table 1), the investigated blends were compacted to different tablet thicknesses to guarantee a comparable tensile strength [33] of 1 MPa. This allows tablets with different dimensions to be compared with each other.

3.4. Disintegration of the investigated tablets

The disintegration times of the liquisolid and the directly compressed tablets are shown in Table 3. Obviously, all formulations (except for formulation LS-N) disintegrated within less than 15 s. This very fast tablet disintegration may be explained by the presence of the superdisintegrant Kollidon® CL [35] as well as microcrystalline cellulose Avicel® leading to an extremely fast water penetration into the tablets caused by wicking and subsequent widening of the pores [36]. Thus, drug release was not hindered by slow disintegration of the dosage form. Tablets containing Neusilin (LS-N) disintegrated within 4.5 min because of the poor disintegration properties of this silicate.

3.5. Drug release from the investigated tablet formulations

Drug release profiles of the conventional and the aerogel tablets as well as the liquisolid compact formulation LS-1 are shown in Fig. 1. It is obvious that drug release from the liquisolid compacts was much faster than that from the conventional tablets although both formulations disintegrated rapidly (Table 3): Within 5 min, only 37% of griseofulvin was released from the conventional tablets as compared to the LS-1 compacts with 95% drug release. Even though the liquisolid compacts LS-1 represent solid dosage forms, the drug is dissolved in the liquid vehicle within the powder matrix. Thus, drug release from LS-1 compacts was solely dependent on the disintegration of the tablets and the miscibility of the liquid portion with the dissolution medium. The comparatively slow drug release from conventional tablets can mainly be explained by the poor water solubility of griseofulvin. Even micronization and thus an increased specific surface area of the drug raw material did not result in acceptably fast drug dissolution.

In comparison with the liquisolid compacts LS-1, the aerogel tablets showed a slightly slower drug release. However, compared to the conventional tablets, the drug release rate from the aerogel tablets was much higher with more than 73% within 5 min. This

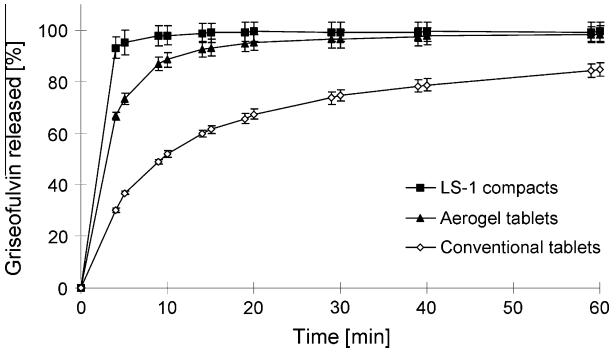

Fig. 1. Drug release profiles of the conventional tablets, the aerogel tablets, and the liquisolid compacts LS-1 (means ± SD; $n = 3$).

faster drug release from hydrophilic aerogels was also observed by Smirnova et al. [10] who investigated different methods for drug release enhancement of griseofulvin, namely micronization of drug by milling, by rapid expansion from supercritical solutions (RESS), and drug adsorption to hydrophilic aerogels. The faster drug release of the aerogel tablets may be explained by both an increase in the specific surface area of the drug resulting from the adsorption to the aerogel microspheres and possibly an amorphous state of the drug. X-ray diffraction patterns confirmed the hypothesis that no crystalline structures of the drug are present in drug-loaded aerogel formulations and no long-range order is established upon adsorption of the drug to silica aerogels [11,30]. The faster drug release from aerogel tablets may also be caused by fast wetting of the hydrophilic aerogel and an immediate collapse of its structure in aqueous media [10,30].

In Fig. 2, drug release profiles of several liquisolid compacts with varying drug contents in the liquid portion are shown. It is apparent that the drug content in the liquid portion had an effect on drug release from liquisolid compacts. With increasing drug content in the liquid portion exceeding the solubility limit and thus a decreasing fraction of dissolved drug in the liquid portion, the release rate decreased. This effect is illustrated in detail in Fig. 3 where the drug content in the liquid portion of the compacts LS-1–LS-10 is plotted versus drug release at 20 min. This decrease in

Table 3
Disintegration times of the investigated tablets (means ± SD, $n = 3$).

Formulation	Conventional tablet	Aerogel tablet	LS-1 compact	LS-2 compact	LS-3 compact	LS-4 compact	LS-5 compact	LS-6 compact	LS-7 compact	LS-8 compact	LS-9 compact	LS-10 compact	LS-N compact
Disintegration time (s)	2 ± 1	5 ± 1	3 ± 3	3 ± 0	11 ± 4	7 ± 0	3 ± 2	7 ± 4	8 ± 5	4 ± 1	7 ± 4	10 ± 3	270 ± 27

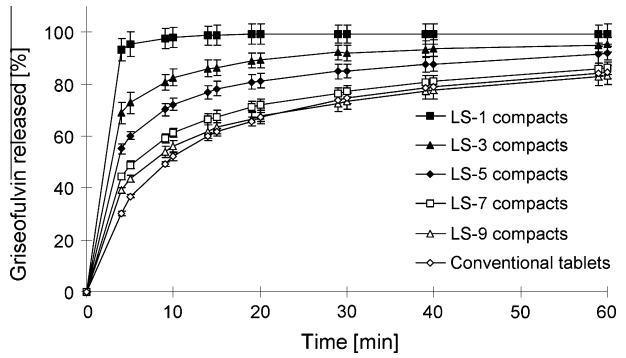

Fig. 2. Drug release profiles of several liquisolid compacts and the conventional tablets (means ± SD; $n = 3$).

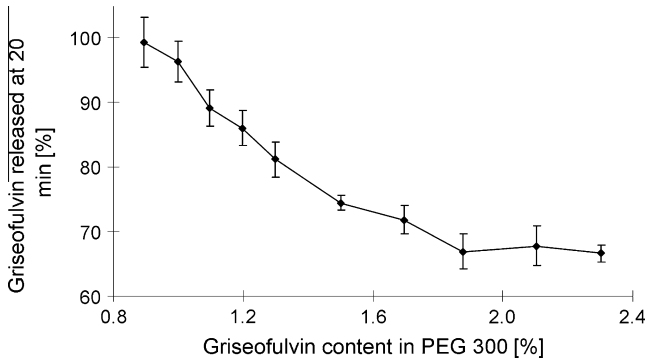

Fig. 3. Influence of the drug content in the liquid portion of liquisolid compacts on the released drug at 20 min (means ± SD; $n = 3$).

drug release is attributed to the increasing amount of undissolved drug.

In Fig. 4, the percentage of released drug from the liquisolid compacts LS-1–LS-10 and the conventional tablets at 20 min is plotted versus the corresponding fraction of dissolved drug in the liquid portion. It is obvious that there was no difference in the percentage of released drug at 20 min between the conventional tablets and the liquisolid compacts LS-8–LS-10 with all formulations showing a release of about 67%. Accordingly, the rising fraction of dissolved drug in these three liquisolid compacts did not lead to the expected increase in drug release. With higher fraction of dissolved drug in the liquid portion above 50%, the released drug at 20 min increased linearly (slope = 0.64, $R^2 = 0.995$). Therefore, the percentage of released drug from liquisolid compacts may be predicted, a fact that was also observed by Spireas et al. [13,14].

In summary, if fast release rates are desired, the liquid portion of liquisolid compacts must contain a high fraction of dissolved drug. However, a liquid portion with a high fraction of dissolved drug might require a high amount of liquid vehicle depending on the solubility of the drug in the liquid vehicle and the required drug dose. As the powder excipients can only adsorb limited amounts of liquid while maintaining good flow and tableting properties, tablet weight will increase with higher amounts of liquid vehicle (Table 1). For instance, the sample unit weight of the fast release formulation LS-1 was more than 2 g, whereas that of LS-10 was only about 800 mg. However, this lighter formulation contained a comparatively high fraction of undissolved drug in the liquid portion and thus showed a significantly lower drug release compared to the heavy formulation LS-1.

As the liquid load factor is dependent on the carrier and coating materials used, a further aim of this study was to optimize the liquisolid technique by replacing the commonly used carrier and coating materials Avicel® and Aerosil® by Neusilin® US2. This magnesium aluminometasilicate with its extremely high specific surface area allowed a considerably higher liquid load factor of 1.58 and thus the production of liquisolid formulations with lower tablet weights. Replacement of Avicel® and Aerosil® by Neusilin® led to a reduction in the weight of the sample unit containing 3 mg of griseofulvin dissolved in PEG 300 from 2026 mg to 600 mg (Table 1).

In Fig. 5, drug release from the liquisolid compacts LS-N and the conventional tablets is shown. It is obvious that the release from the liquisolid compacts LS-N was much faster than that from the conventional tablets. This may be attributed to the above mentioned dissolved state of the drug in these liquisolid compacts. However, in comparison with the liquisolid compacts LS-1 (Fig. 1) containing Avicel® and Aerosil® as carrier and coating materials, respectively, it is interesting that the release from LS-N compacts was slower than that from LS-1 compacts within the first 10 min, although both formulations contained a 0.9% drug solution in PEG 300 as liquid portion. The percentage of griseofulvin released from LS-1 compacts reached 95% already after 5 min, while with LS-N compacts only a release of 82% was observed within this time period. This initially slower release rate from LS-N compacts may be explained by the slower disintegration of LS-N compacts (Table 3) compared with LS-1 compacts, which disintegrated instantaneously. With LS-N compacts, disintegration was the rate-limiting step and thus, drug release may be accelerated by increasing the amount of disintegrant in the formula resulting in faster disintegration.

Even though a tablet of 2 g weight is not applicable, the data presented in this study introduce a general approach how to

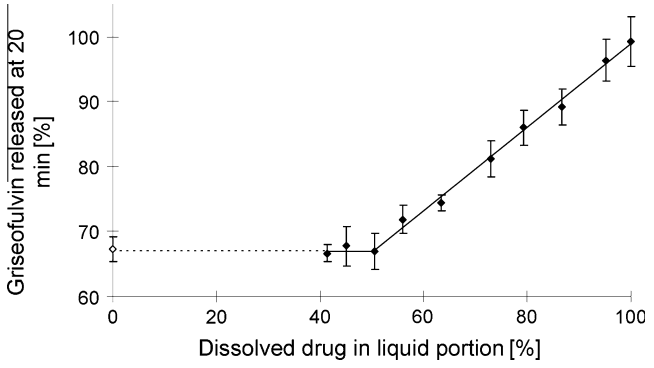

Fig. 4. Influence of the fraction of dissolved drug in the liquid portion of liquisolid compacts on the released drug at 20 min (means ± SD; $n = 3$); ◇ data of the conventional tablets.

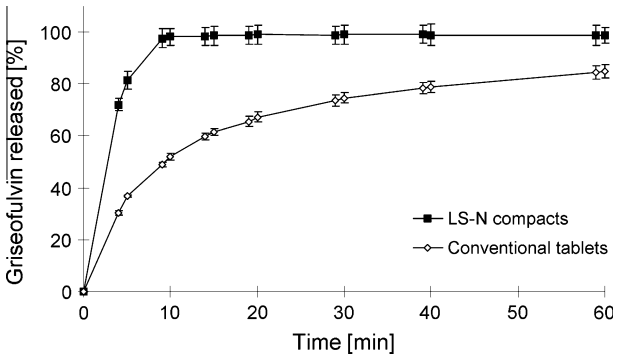

Fig. 5. Drug release profiles of the liquisolid compacts LS-N and the conventional tablets (means ± SD; $n = 3$).

enhance drug release by applying the liquisolid technique and how to minimize tablet weight by application of highly adsorptive excipients. Formation of microsystems by addition of polyvinylpyrrolidone (PVP), hydroxypropyle methylcellulose (HPMC), or polyethylene glycol (PEG 35000) to the liquid portion [24] represents a further alternative for a reduction in the tablet weight.

4. Conclusion

Griseofulvin release from silica aerogel tablets and from liquisolid compacts is faster than that from conventional tablets containing the crystalline drug. Moreover, with liquisolid compacts containing the drug suspended in PEG 300, the release rate increases with rising fraction of dissolved drug in the liquid portion. Highest drug release rates are observed with liquisolid compacts containing a drug solution as liquid portion. Therefore, if the desired drug dose is high and/or the drug solubility in the liquid vehicle is low, a high amount of liquid vehicle is needed which in turn requires high amounts of carrier and coating materials. This results in an increase in tablet weight usually leading to an unacceptably high tablet size. Replacement of the commonly used carrier and coating materials Avicel® and Aerosil®, respectively, by the highly adsorptive silicate Neusilin® allows a considerably higher liquid loading capacity ultimately resulting in lower tablet weights.

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